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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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7590	11/03/2006		EXAMINER	
Robert W. Strozier ROBERT W. STROZIER, P.L.L.C. P.O. Box 429 Bellaire, TX 77402-0429			SMITH, CAROLYN L	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/901,782

Applicant(s)

HARDIN ET AL.

Examiner

Carolyn L. Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2006 and 22 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10,13-19 and 50-99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10,13-19,50-55,57-62,64-69,71-77 and 79-99 is/are rejected.
- 7) ☒ Claim(s) 56,63,70,78 and 79 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's amendments and remarks, filed 6/7/06 and 8/22/06, are acknowledged.

Amended claims 10, 13, 14, and 15 and new claims 57-99 are acknowledged.

Applicant's arguments, filed 6/7/06, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 10, 13-19, and 50-99 are herein under examination.

Claim Objections

Claim 79 is objected to because of the following informality: Claim 79 recites "a site" in singular form in line 2, but later states "are not sites" in plural form on line 8. Appropriate correction is required.

Claims Rejected Under 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

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Claims 10, 13-19 and 79-99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

Applicants point to support for the amended claim limitations on pages 20-21, 40-41, 45-52, 58, and 72-73. There does not appear to be adequate written support for the following limitations: “and where the polymerizing agent lacks 3’ to 5’ exonuclease activity” (claim 10) and “lacking 3’ to 5’ exonuclease activity” (claims 13 (pertaining to polymerase on line 2), 14 (pertaining to T7 DNA polymerase on line 3 and pertaining to the Klenow fragment from E. coli DNA polymerase I on line 4)), and the polymerizing agent “lacking 3’ to 5’ exonuclease activity” (claim 79, line 2). While there is written support for Taq DNA polymerase I lacking 3’ to 5’ exonuclease activity (page 4, first full paragraph and page 40, fourth paragraph) and Taq DNA polymerase I, Sequenase, and reverse transcriptase including HIV-1 reverse transcriptase inherently lack 3’ to 5’ exonuclease activity (see Wisniewski et al. (Journal of Biological Chemistry, 1999, Volume 274, Number 40, pages 28175-28184) and Gardner et al. (Nucleic Acids Research, 2002, Volume 30, Number 2, pages 605-613)), there is no written support regarding this lack of 3’ to 5’ exonuclease activity nor is this activity inherent for T7 DNA polymerase and the Klenow fragment from E. coli DNA polymerase I (see USB Molecular Biology Reagents/Protocols 1992, pages 150 and 152) in the originally filed application, as now stated in amended claims 13 and 14. It is noted that page 72 (fourth paragraph) of the specification states T7 DNA polymerase has exonuclease activity. In addition, there does not appear to be written support for a polymerizing agent and polymerase lacking 3’ to 5’

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exonuclease activity (as stated in instant claims 10, 13, and 79) which encompasses the above-mentioned non-inherent polymerases lacking 3' to 5' exonuclease activity that do not have written support.

There does not appear to be adequate written support for the phrase “where the site comprises a naturally occurring cysteine site or a cysteine replacement site in the polymerizing agent selected so that the site is less than or equal to about 25Å from a tag on each incorporating monomer regions and are not sites having structural/functional importance to proper functioning of the polymerizing agent and is covalently bonded to the cysteine through its SH group” (claim 79) and “the site comprises a naturally occurring cysteine site or a cysteine replacement site in the polymerizing agent selected so that the site is less than or equal to about 25Å from a tag on each incorporating monomer regions and is covalently bonded to the cysteine through its SH group” (claim 89). There does not appear to be adequate written support for “the site is less than or equal to about 15Å from a tag on each incorporating monomer” (claims 80 and 90) and “the site is less than or equal to about 10Å from a tag on each incorporating monomer” (claims 81 and 91). Written basis is provided for a cysteine replacement site (page 46, third paragraph), but not “naturally occurring cysteine site” which differs in scope. While there is written basis for distance separating tags to be within about 25Å, 15Å, and 10Å (page 18, last paragraph and page 20, second paragraph), there does not appear to be written support for “the *site* is less than or equal to about 25Å from a tag on each incorporating monomer regions”, “the *site* is less than or equal to about 15Å from a tag on each incorporating monomer”, and “the *site* is less than or equal to about 10Å from a tag on each incorporating monomer” which differ in scope. Written basis is provided for cysteine replacement preferred sites that are not in contact with other

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proteins, do not alter conformation of the polymerase, and are not involved in protein function (page 46, third paragraph); however, this does not support the phrase “are not sites having structural/functional importance to proper functioning of the polymerizing agent” which differs in scope. Written basis is provided for “cysteine residue includes a tag covalently bonded thereto through the SH group”; however this does not provide adequate written support for “is covalently bonded to the cysteine through its SH group” which is broader in scope as it does not state what is covalently bonded to the cysteine or whose “SH group”.

Because the introduction of “and where the polymerizing agent lacks 3’ to 5’ exonuclease activity” (claim 10), “lacking 3’ to 5’ exonuclease activity” (claims 13-14), “the polymerizing agent lacking 3’ to 5’ exonuclease activity” (claim 79), “where the site comprises a naturally occurring cysteine site or a cysteine replacement site in the polymerizing agent selected so that the site is less than or equal to about 25Å from a tag on each incorporating monomer regions and are not sites having structural/functional importance to proper functioning of the polymerizing agent and is covalently bonded to the cysteine through its SH group” (claim 79), “the site comprises a naturally occurring cysteine site or a cysteine replacement site in the polymerizing agent selected so that the site is less than or equal to about 25Å from a tag on each incorporating monomer regions and is covalently bonded to the cysteine through its SH group” (claim 89), “the site is less than or equal to about 15Å from a tag on each incorporating monomer” (claims 80 and 90), and “the site is less than or equal to about 10Å from a tag on each incorporating monomer” (claims 81 and 91) lack written basis, filed on 8/22/06, these phrases are considered to be NEW MATTER. Claims 15-19, 82-88 and 92-99 are also rejected due to their direct or indirect dependency from claims 10, 13, 14, 79, and 89. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 79-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Claims 79 and 89 (last line of each) recite the limitation "the cysteine". There is insufficient antecedent basis for this limitation in these claims. While there is prior mention of a cysteine site or cysteine replacement site, there is not previous mention of an actual cysteine. Clarification of this issue via clearer claim wording is requested. Claims 80-88 and 90-99 are also rejected due to their dependency from claims 79 and 89.

Claims 79 and 89 recite the phrase "is covalently bonded to the cysteine through its SH group" (last line) which is vague and indefinite. It is unclear what is covalently bonded to the cysteine which may be the polymerizing agent, the site, or the tag. It is unclear if the "its" is referring to the cysteine, polymerizing agent, or the site. Clarification of this issue via clearer claim wording is requested. Claims 80-88 and 90-99 are also rejected due to their dependency from claims 79 and 89.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10, 13-18, 50-55, 57-62, 64-69, and 71-77 are rejected under 35 U.S.C. 102(e) as being anticipated by Korlach et al. (US 2006/0078937 A1) in light of Wisniewski et al. (Journal of Biological Chemistry, 1999, Volume 274, Number 40, pages 28175-28184) and Gardner et al. (Nucleic Acids Research, 2002, Volume 30, Number 2, pages 605-613). This rejection is necessitated by amendment.

Korlach et al. disclose a composition comprising a polymerizing agent including a molecular tag covalently bonded to a site on the polymerizing agent and a monomer including a molecular tag, where at least one of the tags has a fluorescence property that undergoes a change before, during and/or after each of a sequence of monomer incorporations due to an interaction between the polymerizing agent tag and the monomer tag (claim 62), as stated in instant claim 10. Korlach et al. disclose a composition wherein the polymerizing agent is a polymerase or reverse transcriptase (claim 63), as stated in instant claims 13 and 72. Korlach et al. disclose a composition wherein the polymerase is selected from the group of Taq DNA polymerase, T7 DNA polymerase, Sequenase, and the Klenow fragment from E. coli DNA polymerase (claim 64), as stated in instant claims 14 and 73. Korlach et al. disclose a composition wherein the reverse transcriptase comprises HIV reverse transcriptase (claim 65), as stated in instant claims

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15 and 74. Korlach et al. disclose a composition wherein each of the monomers comprises a deoxynucleotide triphosphate (dNTP) and the monomer tag is covalently bonded to the α , β , or γ phosphate group of each dNTP (claim 66 and paragraphs 0064-0067), as stated in instant claim 16 and the terminal phosphate of the monomer, as stated in instant claims 71 and 75. Korlach et al. disclose a composition wherein the tags comprise fluorescent tags, and the fluorescence property comprises an intensity, wavelength, and/or frequency of emitted fluorescent light (claim 67), as stated in instant claims 17 and 76. Korlach et al. disclose a composition wherein the fluorescence property is fluorescence resonance energy transfer (FRET) where either the monomer tag of the polymerase tag comprises a donor and the other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity (claim 68), as stated in instant claims 18 and 77. Korlach et al. disclose a composition wherein the polymerase comprises Taq DNA Polymerase having a tag attached to an amino acid position at a specific amino acid of the Taq DNA polymerase that is less than 60 Å from an incorporating nucleotide (claim 69). Korlach et al. disclose a composition comprising a polymerizing agent including a molecular tag covalently bonded to a site on the polymerizing agent and a deoxynucleotide triphosphate (dNTP) including a molecular tag covalently bonded to the β or γ phosphate group of the dNTP, where at least one of the tags has a fluorescence property that undergoes a change before, during and/or after each of a sequence of monomer incorporations due to an interaction between the polymerizing agent tag and the monomer (claim 70), as stated in instant claims 50, 57, and 64. Korlach et al. disclose a composition wherein the polymerizing agent is a polymerase or reverse transcriptase (claim 71), as stated in instant claims 51, 58, and 65. Korlach et al. disclose a composition wherein the polymerase is selected from the group consisting of Taq DNA

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polymerase, T7 DNA polymerase, Sequenase, and the Klenow fragment from E. coli DNA polymerase (claim 72), as stated in instant claims 52, 59, and 66. Korlach et al. disclose a composition wherein the reverse transcriptase comprises HIV reverse transcriptase (claim 73), as stated in instant claims 53, 60, and 67. Korlach et al. disclose a composition wherein the tags comprise fluorescent tags, and the fluorescence property comprises an intensity, wavelength, and/or frequency of emitted fluorescent light (claim 74), as stated in instant claims 54, 61, and 68. Korlach et al. disclose a composition wherein the fluorescence property is fluorescence resonance energy transfer (FRET) where either the monomer tag of the polymerase tag comprises a donor and the other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity (claim 75), as stated in instant claims 55, 62, and 69. Korlach et al. disclose a composition wherein the polymerase comprises Taq DNA Polymerase having a tag attached to an amino acid position at a specific amino acid of the Taq DNA Polymerase, that is less than 60 Å from an incorporating nucleotide (claim 76). Korlach et al. disclose the sequencing method of the present invention can be carried out using polymerase and no exonuclease (paragraph 0019). It is noted that Korlach et al. do not specifically state the inherent characteristics of HIV-1 reverse transcriptase, Sequenase, and Taq DNA polymerase I in that they lack 3' to 5' exonuclease activities. Wisniewski et al. (page 28175, col. 2, first paragraph) and Gardner et al. (page 606, col. 1, last paragraph) recite these inherent characteristics. Wisniewski et al. and Gardner et al. are not being used as prior art, but rather to document these inherent characteristics of HIV-1 reverse transcriptase, Sequenase, and Taq DNA polymerase I.

Korlach et al. in light of Wisniewski et al. and Gardner et al. anticipate the limitations in claims 10, 13-18, 50-55, 57-62, 64-69, and 71-77.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 79-87 and 89-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korlach et al. (US 2006/0078937 A1) in light of Wisniewski et al. and Gardner et al. as applied to claims 10, 13-18, 50-55, 57-62, 64-69, and 71-77 above, and further in view of Schneider et al. (US 6,982,146 B1). This rejection is necessitated by amendment.

Korlach et al. in light of Wisniewski et al. and Gardner et al. describe the limitations of 10, 13-18, 50-55, 57-62, 64-69, and 71-77, as stated in the 35 USC 102 rejection above. Korlach et al. describe the limitations in dependent claims 82-87 and 92-98, as documented in the 35 USC 102 rejection above. Korlach et al. do not describe where the site comprises a naturally occurring cysteine site in the polymerizing agent selected so that the site is less than or equal to

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about 25Å, 15Å, or 10Å from a tag on each incorporating monomer regions and are not sites having structural/functional importance to proper functioning of the polymerizing agent and is covalently bonded to the cysteine through its SH group (claims 79-81 and 89-91).

Schneider et al. describe attachment of fluorophores to a polymerase (col. 19, line 57 to col. 20, line 35). Schneider et al. describe using thiol-reactive probes to generate fluorescently-labeled polymerase where the thiol (SH) groups that are present in the cysteine residues react with the fluors to yield chemically stable thioesters (col. 20, second paragraph), noting that fluorescently-labelled polymerases have high fluorescent yield and retain critical features of the polymerase thus preserving the function of the polymerase (col. 20, lines 26-32) as well as the limited distance of 10Å between a donor fluorophore on a polymerase and a target acceptor fluorophore on a nucleotide without collateral stimulation of other acceptor fluorophores (col. 9, fifth paragraph), as stated in instant claims 79-81 and 89-91.

Korlach et al. state a need to provide a method for sequencing nucleic acid molecules that requires only polymerase activity, without the use of blocking substituents, resulting in greater simplicity, easier miniaturizability, and compatibility to parallel processing of a single-step technique (paragraph 0013). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of Korlach et al. by attaching the molecular tag to a cysteine site as taught by Schneider et al. where the motivation would have been to meet today's demand for rapid, high-throughput sequencing and accurately sequence nucleic acids at the molecular scale at high speed and long reading lengths, without requiring the labor intensive use of electrophoresis or complex liquid pumping systems, via fluorescently-labeled polymerases that retain the ability to synthesize a complementary strand and have a high

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fluorescent yield, as stated by Schneider et al. (col. 3, fifth paragraph and col. 20, fifth paragraph) and Korlach et al. (paragraphs 0004-0005 and 0010).

Thus, Korlach et al. in light of Wisniewski et al. and Gardner et al. and in view of Schneider et al. make obvious claims 10, 13-18, 50-55, 57-62, 64-69, 71-77, 79-87, and 89-98.

Applicants summarize the rejection. Applicants submit that they formally antedate Korlach et al. as it pertains to the use of beta phosphate, gamma phosphate, and/or terminal phosphate labeled dNTPs in single molecule sequencing, and request withdrawal of the 35 USC 102 rejection as it relates to claims 50-55, 57-78, and 89-99. It is noted that claims 57-78 and 89-99 are new claims and therefore were not previously rejected. It is noted that the 35 USC 102 rejection of claims 10, 13-18, 50-55, 57-62, 64-69, and 71-77 is necessitated by amendment for the reasons given above. Applicants submit that the present invention was made before May 17, 2000, and the Applicants' attorney can attest via documentary evidence that the present invention was invented prior to May 17, 2000, which is the date of filing of the Korlach 09/572530 application. These statements are found unpersuasive as they are insufficient allegations that lack any factual support. It is noted that filing a declaration under 37 CFR § 1.131 would be considered improper, because it is a potential interference with the claims of the prior art reference. Applicants are advised to file the appropriate papers under 37 CFR § 41.202 or § 41.203, as appropriate.

Applicants argue that Korlach et al.'s provisional application does not disclose beta and/or gamma phosphate labeled dNTPs. This statement is moot as the filing date of Korlach et al.'s 09/572530 application (May 17, 2000) is sufficient for making the 35 USC 102(e) rejection above. Applicants argue that Korlach et al. do not disclose terminal phosphate labeled nucleotides. This statement is found unpersuasive as Korlach et al. disclose a monomer tag covalently bonded to the α , β , or γ phosphate group of each dNTP (claim 66 and paragraphs 0064-0067).

Applicants reiterate arguments regarding antedating the prior art reference which were found unpersuasive as stated above. Applicants request withdrawal of the 35 USC 102(e) rejection of claims 50-55, 57-78, and 89-99. It is noted that claims 57-78 and 89-99 are new claims and therefore were not in the previous rejection. It is noted that the 35 USC 102 rejection of claims 10, 13-18, 50-55, 57-62, 64-69, and 71-77 is necessitated by amendment for the reasons given above.

Applicants summarize Korlach et al.'s (May 17, 2000) application (now US 7,056,661) and argue that this application does not support using beta and/or gamma phosphate labeled dNTPs in the context of FRET detection of incorporating events. This statement is found unpersuasive as US 7,056,661 makes reference to using beta and gamma phosphate labeled dNTPs (col. 14, last paragraph to col. 15, first paragraph) and FRET (col. 26).

Applicants argue that US 6,982,146 (Schneider et al.) does not anticipate or render obvious claims 50-55, 57-78, and 89-99 because of failure to disclose labeling dNTP at the β and/or γ phosphate or terminal phosphate. This statement is found moot as Korlach et al. disclose these limitations (claim 66 and paragraphs 0064-0067).

Applicants reiterate that they have formally antedated Korlach et al.'s 09/572530 application as it pertains to beta, gamma, and terminal phosphate labeled dNTPs. This statement is again found unpersuasive for reasons given above. Applicants submit that Korlach et al.'s provisional application does not recite beta, gamma, and terminal phosphate labeled dNTPs. This statement is again found moot for reasons already given above. Applicants argue that the provisional does not render claims 50-55, 57-78, and 89-99 obvious and summarize the provisional application. These statements are considered moot as an obvious rejection for this provisional application was not made.

Applicants note amendments made to claims 10 and 13-18. Applicants argue that Korlach et al. do not disclose polymerases lacking 3' to 5' exonuclease activity. This statement is found unpersuasive as this activity is an inherent characteristic for Sequenase, Taq DNA polymerase I, and reverse transcriptase, including HIV-1 reverse transcriptase (see Wisniewski et al. (page 28175, col. 2, first paragraph) and Gardner et al. (page 606, col. 1, last paragraph)). Applicants argue that Schneider et al. do not disclose polymerases lacking 3' to 5' exonuclease activity. This statement is found moot as this activity is inherent for Sequenase, Taq DNA polymerase I, and reverse transcriptase, including HIV-1 reverse transcriptase, as stated above.

Applicants argue that Korlach et al. nor Schneider et al. render claims 79-88 obvious as there is no teaching in these references regarding polymerases lacking 3' to 5' exonuclease activity, the proper placement of the tag on the polymerizing agent that should be less than or equal to 25 Å from the incorporating monomers, or that the site be located on a site that is not important to the proper functioning of the polymerizing agent. These statements are unpersuasive as the characteristic of polymerases lacking 3' to 5' exonuclease activity is an

inherent characteristic for Taq DNA polymerase I, Sequenase, and reverse transcriptase (including HIV-1 reverse transcriptase) and the other limitations listed above are described by Schneider et al. (col. 19-20).

Applicants submit that they have fully responded to the Examiner's Final Office Action. It is noted that the previous Office Action was a non-final Office Action.

Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

Claims 56, 63, 70, and 78 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 56, 63, 70, and 78 recite specific amino acid positions of SEQ ID NO: 11 from Taq DNA polymerase I for attachment to a tag which are not disclosed in the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811.

October 26, 2006


Carolyn Smith
Examiner
AU 1631